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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/455,683	05/31/95	BELL G	ARCD:177/WIM

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EXAMINER	
TENG,S	

ART UNIT	PAPER NUMBER
1646	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/455,683	Applicant(s) Bell et al.
	Examiner Sally Teng	Group Art Unit 1646

☒ Responsive to communication(s) filed on *Mar 30, 1998*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *47-90* is/are pending in the application.

Of the above, claim(s) *53-58, 60-62, and 68-80* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *47-49, 51, 59, 63-67, 81, and 83-90* is/are rejected.

☒ Claim(s) *50, 52, and 82* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Claims 47-90 are pending in the instant application.

Applicant elected the invention of Group I and chimeric opioid receptors as the species in Paper No. 12.

Claims 53-58, 60-62, and 68-80 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected species. Election was made **without** traverse in Paper No. 12.

2. Acknowledgment is made of applicant's claim for foreign priority based on application PCT/US94/05747 filed on May 20, 1994. It is noted, however, that applicant has not filed a certified copy of the application as required by 35 U.S.C. 119(b).

3. The rejection of claims 47-51 and 63-65 under § 112, second paragraph is withdrawn.

The rejection of claims 47-51 under § 112, first paragraph, is withdrawn in favor of a new rejection as set forth below.

The rejection of claims 59 and 63-65 under § 112, first paragraph, is withdrawn in favor of a new rejection as set forth below.

The rejection of claim 47 under § 102(a) as being anticipated by Evans et al. or Kieffer et al. is withdrawn.

The rejection of claim 59 under § 102(b) as being anticipated by Ahmed et al. is withdrawn.

4. It is suggested that claims 82 and 83 be amended to refer to the process of claim 47, since claim 47 recites the process steps.

5. Claim 59 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 59 is confusing. The preamble and the last step are directed to isolating a substance that can interact as a kappa opioid receptor; however, it seems that the claimed process requires contacting the opioid receptor with a candidate substance that has already been isolated (step b). It is no longer clear as to whether the opioid receptor is contacted with an isolated candidate. Is the candidate substance in step b a composition comprising different test compounds?

It is also suggested that step d be amended to "isolating said substance, if the substance has the ability to interact with the opioid receptor."

6. Claims 47-49, 51, 81, 83, and 84-90 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for chimeric opioid receptors comprising the second extracellular loop of the kappa opioid receptor or the third extracellular loop of the delta opioid receptor and for opioid receptors comprising the second extracellular loop of the kappa opioid receptor or the third extracellular loop of the delta opioid receptor, does not reasonably provide enablement for any chimeric opioid receptor or any opioid receptor peptides. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

Claims 47-49 and 51 are directed to a method of screening for a substance that interacts with an opioid receptor using a broad genus of chimeric opioid receptors that do not comprise the second extracellular loop of the kappa opioid receptor or the third extracellular loop of the delta opioid receptor, and claims 81 and 83-90 are directed to the same method but encompass the use of a broad genus of opioid receptor peptides that do not comprise the required extracellular domains for ligand binding. The claims have been amended to specifically recite detecting the ability of the substance to interact with an opioid receptor. The specification teaches that the second extracellular loop of the kappa opioid receptor and the third extracellular loop of the delta opioid receptor are required for specific ligand binding for each of the opioid receptors respectively. Therefore, the use of chimeric opioid receptors and opioid receptor peptides lacking these specific loops to perform the recited methods would not enable the skilled artisan to determine whether a substance interacts specifically with a kappa opioid receptor or a delta opioid receptor. These chimeric opioid receptors and opioid receptor peptides lacking the required extracellular loops would not interact with ligands even if they are specific for the kappa or delta opioid receptor.

Applicant contends that since opioid receptors have substantial structural similarities, the specification enables the skilled artisan to obtain chimeric opioid receptors from any opioid

receptor. However, as taught by the specification, each opioid receptor has a different extracellular loop for ligand interaction. The specification only teaches that the second extracellular loop of the kappa opioid receptor and the third extracellular loop of the delta opioid receptor are required for ligand binding for each of the opioid receptor, respectively. Chimeric opioid receptors comprising regions that are not required for ligand binding cannot be used in the recited assay to determine whether a substance interacts with an opioid receptor. Further, the specification does not disclose other opioid receptors or their structural domains that are essential for specific ligand binding. Accordingly, even if the structures of opioid receptors are substantially similar, it does not enable the skilled artisan to predict as to which domains or loops of a specific opioid receptor is required for ligand binding. Thus, the specification does not enable the scope of the claims.

7. Claims 59 and 63-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims have been amended to recite a process for isolating a substance that act as an agonist of a kappa opioid receptor.

First of all, the claims as they stand are directed to a method of isolating a substance that is a specific agonist of a kappa opioid receptor; however, the recited process steps require the use

the substance in isolated form. In order for the skilled artisan to determine whether a substance is a specific agonist of a kappa opioid receptor, step b of the recited process steps must be performed with an isolated substance. If the candidate substance of step b is not an isolated compound or is a composition comprising several candidates, the skilled artisan would not be able to determine which compound is an agonist for the kappa opioid receptor.

Secondly, the preamble is directed to a process for isolating a substance that is an agonist for the kappa opioid receptor, while step a recites providing any chimeric opioid receptor. In order to determine whether a substance interacts with a kappa opioid receptor, the chimeric opioid receptor must comprise at least the second extracellular loop of the kappa opioid receptor. As explained above, the specification teaches that the second extracellular loop of the kappa opioid receptor is essential for specific ligand interaction. Chimeric opioid receptors lacking the second extracellular loop of the kappa opioid receptor would not enable the skilled artisan to determine whether a substance is a kappa opioid receptor, since they are not able to interact with ligands, even if they are specific kappa opioid agonists.

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 47, 59, and 84-90 are rejected under 35 U.S.C. 102(b) as being anticipated by Ahmed et al.

The rejection of record, as set forth in paragraph 10 of the last Office action, is maintained as applied to claims 47 and 59, and is now applied to new claims 84-90. Claims 84-90 encompass the use of the full length human opioid receptor in the claimed process and therefore are included under the present rejection. Also, the nucleic acids encoding the mouse and the human opioid receptors ~~are~~ have high sequence identity. Thus, any 40, 55, or 70 contiguous bases of SEQ ID NO: 1 are also present in the nucleic acid encoding the human opioid receptor.

Although claim 59 has been amended to a method of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor using a human kappa opioid receptor, the claim does not include method steps that distinguishes the claimed method from the assay for determining kappa opioid receptor specific agonist disclosed in the reference.

Claim 81 uses close language in reciting the amino acid sequence of the human opioid receptor. Therefore, it is not included in the present rejection.

Applicant's arguments filed March 30, 1998, have been fully considered but they are not persuasive.

Applicant urges that Ahmed does not contemplate chimeric opioid receptor polypeptides or disclose the sequences of the specific kappa opioid receptor. It is agreed that Ahmed does not teach chimeric opioid receptor. However, the claims are not limited to the use of the chimeric opioid receptor. The claims encompass the use of the full length human kappa opioid receptor. While it is agreed that Ahmed does not disclose the amino acid sequence of the opioid receptor, it is pointed out the amino acid sequence of a protein is an inherent property of the protein. In the

absence of evidence that the human kappa opioid receptor of Ahmed is structurally and functionally distinct from the human kappa opioid receptor of the present application, the claims are anticipated by Ahmed. The burden is upon the applicant to show that the disclosed human kappa opioid receptor is patentably distinct from the human kappa opioid receptor of the present application (*In re Swinehart* 58 CCPA 1027, 439 F.2d 210, 169 USPQ 226 (1971)).

10. Claims 47 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al.

The rejection of record as set forth in paragraph 11 of the last Office action is maintained as applied to claims 48 and 49 and is now applied to amended claims 47 and 48. The claims encompass the use of a chimeric opioid receptor comprising a portion of the delta opioid receptor in a ligand screening assay. Claims 47 and 48 do not specify a specific portion of the delta opioid receptor.

Applicant's arguments filed March 30, 1998, have been fully considered but they are not persuasive.

Applicant urges that the rejection is improper because Evans in view of Frielle does not suggest the chimeric opioid receptor polypeptide or that the claimed invention would be successful. It is pointed out that the claims as they stand are not limited to chimeric receptors having specific amino acid sequences of the delta opioid receptor. Although neither of the cited references by itself discloses chimeric delta opioid receptor, the combination of the two references

provides motivation and reasonable expectation of success in obtaining chimeric delta opioid receptor. Evans discloses the primary structure of the delta opioid receptor, and Frielle teaches method steps for obtaining chimeric G-protein coupled receptors and using them in ligand binding assays for determining the structure/function relationship of the receptor. Accordingly, it would have been *prima facie* obvious to the skilled artisan at the time the invention was made to modify the delta opioid receptor of Evans by following the teachings of Frielle to obtain chimeric delta opioid polypeptides and to use them in ligand binding assays to determine which region of the delta opioid receptor is essential for specific ligand binding.

It is agreed that Frielle's work on β-adrenergic receptors would not motivate the skilled artisan to use chimeric delta opioid receptor comprising the third extracellular loop in the disclosed assay. However, the claims as they stand are not directed to the use of chimeric delta opioid receptors having the third extracellular loop or having a specific region that interacts with ligands in the disclosed assays. The claims broadly encompass a broad genus of chimeric delta opioid receptor. Claims that are limited to chimeric delta opioid receptor comprising the third extracellular loop are not included in the present rejection.

11. Claims 50, 52, and 82 are objected to as depending from a rejected base claim.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally Teng, Ph.D., whose telephone number is (703) 308-4230. The examiner can normally be reached on Mon.-Fri. from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957.

Official papers filed by fax should be directed to (703) 305-3014. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June 26, 1998

Sally Teng

SALLY TENG
PRIMARY EXAMINER